4.2 Bladder cancer

4.2.1 The size of the planning target volume (PTV) is critical to any discussion of dose and fractionation. Some centres use a two-phase (large pelvic volume/small bladder volume) approach, although there is no robust evidence for this approach improving survival outcomes for patients (Level 4). There is no published evidence using fraction sizes other than 1.8–2.0 Gy for this approach (Level 3). All of the dose-fractionation regimens discussed below are based on the assumption that the PTV is < 1000 ml and that 3-D image based planning techniques are used. There is also increasing use of adaptive radiotherapy techniques for bladder treatment using a ‘plan of the day’ based on imaging prior to delivery of each fraction. The fractionation evidence has not been tested in this setting but there is no reason to believe that the recommendations below do not apply to the adaptive setting also.

Conventional fractionation (dose-per-fraction 1.8–2.0 Gy)

4.2.2 The radiotherapeutic regimens used in trials comparing radiotherapy to surgery for bladder cancer have been delivered using either a conventional regimen of 60–64 Gy in 30–32 fractions over 6–6.5 weeks or hypofractionated radiotherapy of 52.5 to 55 Gy in 20 fractions (level 2++)

Hyper-fractionation (dose-per-fraction 1.5 Gy or less)

4.2.3 Two published trials compare hyper-fractionation (with doses of 1–1.2 Gy per fraction) to conventionally fractionated treatment. Pooled analysis suggests a significant benefit from hyper-fractionation with a 17% (95% confidence interval, 6–27%) improvement in the rate of local control. However, the regimens in both arms of these studies used split courses with overall treatment times of 8 weeks. This approach would no longer be considered acceptable in a control arm (level 1+).

Accelerated fractionation

4.2.4 There was no evidence of clinical benefit from 60.8 Gy in 32 fractions given using 2 fractions per day of 1.9 Gy over a treatment time of 26 days when compared to a standard regime of 64 Gy in 32 fractions over 45 days. The shorter regimen was associated with a higher rate of intestinal toxicity (level 1+ evidence).

Hypo-fractionation (doses-per-fraction ≥ 2.5 Gy)

4.2.5 The two UK-based randomised controlled trials published in the last five years allowed the use of both conventional (60 Gy in 30 fractions) and hypofractionated radiotherapy (55 Gy in 20 fractions). Although neither study was powered to detect a difference in outcome based on dose and fractionation, there was no difference seen between conventional and hypofractionated radiotherapy.

Partial Bladder irradiation

4.2.6 Partial bladder radiotherapy has been studied in two UK-based trials. A trial from Manchester compared whole bladder radiotherapy 52.5 Gy in 20 fractions with partial bladder irradiation of 57.5 Gy in 20 fractions and 55 Gy in 16 fractions. There was no significant difference in local control at 5 years between the three groups and late toxicity was similar in all three arms (level 1). The BC2001 sub-study compared whole bladder high dose irradiation with reduced high-dose volume radiation therapy. There was no difference in loco-regional recurrence, late toxicity and overall survival between the two groups (level 1-).

Radical radiotherapy with radiosensitisation

4.2.7 Two UK-based randomized controls trials have demonstrated that radical radiotherapy with a radiosensitiser improves outcomes compared to radiotherapy alone. BC2001 compared radical radiotherapy alone with radical radiotherapy given concurrently with
mitomycin C and 5-Fluorouracil with the chemoradiotherapy arm showing significantly better two year loco-regional recurrence rates of 67% vs 54%. BCON compared radical radiotherapy alone to radical radiotherapy given concurrently with carbogen and nicotinamide with a significant improvement in 3 year overall survival in the experimental arm of 13%. (Level 1+). Some centres within the UK use a weekly gemcitabine chemoradiation protocol based on a multicenter phase II study which has shown acceptable toxicity and comparable outcomes to those in the literature (3 year overall survival of 75% and 88% achieving a complete endoscopic response at first check cystoscopy) (level 2++).

For radical radiotherapy to the bladder only, regimens of 52.5-55 Gy in 20 daily fractions and 60–64 Gy in 30–32 daily fractions are effective when using modern radiotherapy techniques (Grade B). There is robust evidence that radiotherapy with a radiosensitiser improves outcomes for patients with organ-confined muscle-invasive bladder cancer (Grade A). ¹⁵

Palliative radiotherapy for bladder cancer

4.2.8 The MRC (Medical Research Council) randomised trial BA09 clearly established that 21 Gy in 3 fractions on alternate weekdays in 1 week (4–6 elapsed days) is as effective as 35 Gy in 10 fractions in 2 weeks in palliating symptoms in patients with bladder cancer.²⁸ There was no statistically significant difference in the rate of symptom relief (64% versus 71%; \( p = 0.192 \); 95% confidence interval for the 7% rate difference, −2% to +13%), nor was there any significant difference in the duration of symptomatic relief (level 1+ evidence). Other palliative regimes which are in use in the UK are 20 Gy in 5 fractions and 30 – 36 Gy in 5-6 fractions over 5-6 weeks (level 2-). These regimes are also used for frail patients not fit for radical radiotherapy treatment.

For very frail patients, a 6–8-Gy single fraction of pelvic radiotherapy often provides symptomatic relief (level 4).

For the palliation of local symptoms from bladder cancer, 21 Gy in 3 fractions on alternate days in 1 week is the regimen of choice (Grade A).

A single fraction of 6–8 Gy may provide useful palliation in patients who are unfit for the recommended regimen (Grade D).
References


